IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of Goddard et al	)	Examiner: Nancy Vogel
Serial No. 10/677,471	)	Group Art Unit: 1636
Filed: October 2, 2003	)	Confirmation No. 1021
Title: SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME	)	Attorney's Docket No. 10466/484

DECLARATION OF AUDREY GODDARD, Ph.D., PAUL J. GODOWSKI, Ph.D., J. CHRISTOPHER GRIMALDI, AUSTIN L. GURNEY, Ph.D., DANIEL TUMAS, Ph.D. AND WILLIAM I. WOOD, Ph.D. UNDER 37 CFR § 1.131

MAIL STOP AMENDMENT
The Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

We, Audrey Goddard, Ph.D., Paul J. Godowski, Ph.D., J. Christopher Grimaldi, Austin Gurney, Ph.D., Daniel Tumas, Ph.D. and William I. Wood, Ph.D. declare and say as follows:

1. We are the inventors of the above-identified application.

2. At the time the present invention was made, one of the inventors, Daniel Tumas, Ph.D., was responsible for overseeing the testing of novel polypeptides, including the polypeptide PRO361, in an assay of inhibitory activity in the mixed lymphocyte relation (MLR) (Assay #67, Example 34). This assay is used to find agents that are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

3. The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12, edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO_2) and then washed and resuspended to $3x10^6$ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50:1 of irradiated stimulator cells, and

50:1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO_2 for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mC/well; Amersham). After 6 hours the cells are washed 3 times and then the update of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to $1x10^7$ cells/ml of assay media. The assay is then conducted as described above.

Any decrease below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein. The results are indicative of the utility of the PRO polypeptides

in therapeutic applications where suppression of an immune response is beneficial.

4. Copies of pages from an internal database showing the positive results for the PRO361 polypeptide (SEQ ID NO: 83), identified by Pin number PIN996-1, in Assay #67 are attached to this declaration (with dates redacted) as Exhibit A. These experiments were performed and the results were obtained in the United States prior to August, 1999.

5. Exhibit A clearly shows that the polypeptide designated PRO361 was tested, and its ability to inhibit the mixed leukocyte reaction was determined prior to August, 1999. .

6. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

A. Goddard Audrey Goddard, Ph.D.	1/12/08 Date
Paul J. Godowski, Ph.D.	Date
J. Christopher Grimaldi	Date
Austin L. Gurney, Ph.D.	Date
Daniel Tumas, Ph.D.	Date
William I. Wood, Ph.D.	Date

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Audrey Goddard, Ph.D.	Date
Paul J. Godowski, Ph.D.	12/19/07 Date
J. Christopher Grimaldi	Date
Austin L. Gurney, Ph.D.	Date
Daniel Tumas, Ph.D.	Date
William I. Wood, Ph.D.	Date

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Audrey Goddard, Ph.D.	Date
Paul J. Godowski, Ph.D.	Date
J. Christopher Grimaldi	3/31/08 Date
Austin L. Gurney, Ph.D.	Date
Daniel Tumas, Ph.D.	Date
William I. Wood, Ph.D.	Date

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Audrey Goddard, Ph.D.	Date
Paul J. Godowski, Ph.D.	Date
J. Christopher Grimaldi	Date
Austin L. Gurney, Ph.D.	Date
Daniel Tumas, Ph.D.	February 14, 2006 Date
William I. Wood, Ph.D.	Date

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Daniel Tumas, Ph.D.	Date
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Paul J. Godowski, Ph.D.	Date
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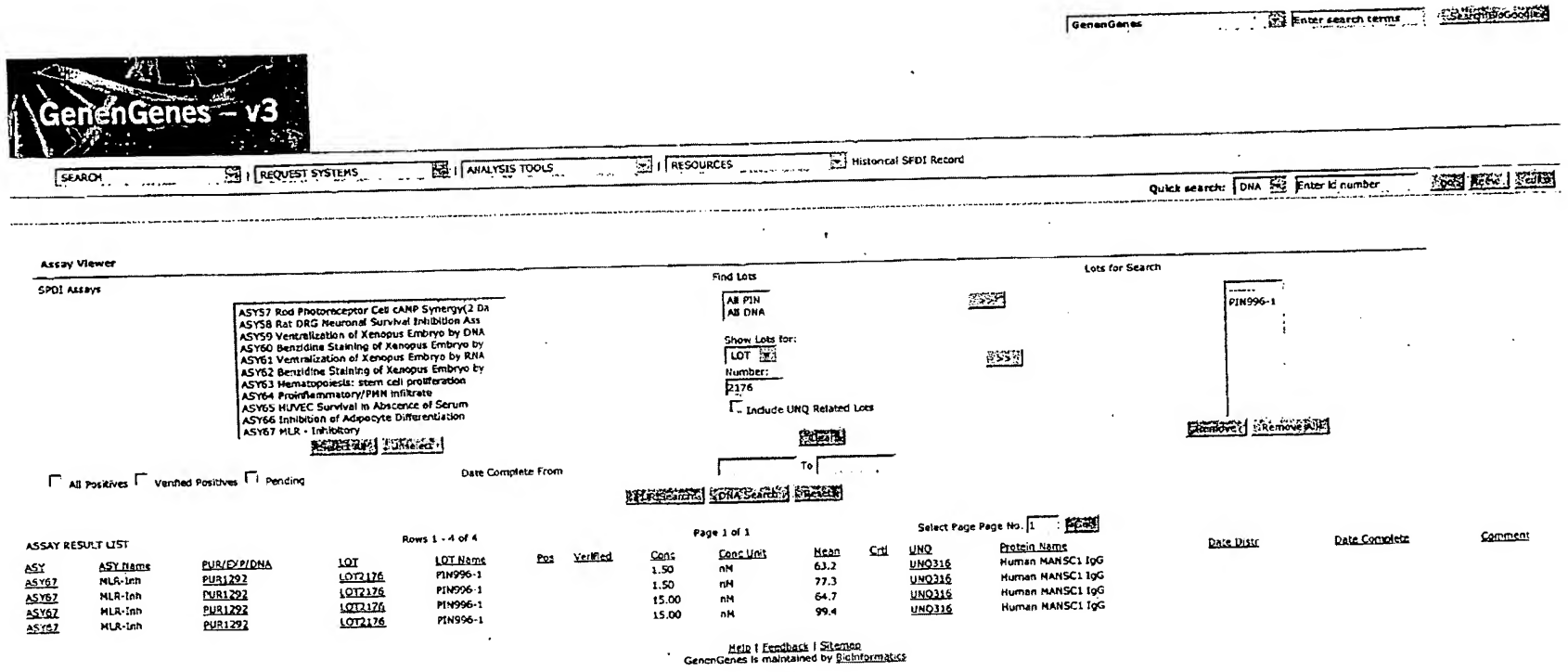
Austin L. Gurney, Ph.D.	Date
Daniel Tumas, Ph.D.	Date
William I. Wood, Ph.D.	12/14/17 Date

EXHIBIT A


GenenGenes
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ANALYSIS TOOLS
RESOURCES
Historical SPDI Record
Quick search:
DNA
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Assay Viewer
SPDI Assays
ASY57 Rod Photoreceptor Cell cAMP Synergy(2 Da
ASY58 Rat DRG Neuronal Survival Inhibition Ass
ASY59 Ventralization of Xenopus Embryo by DNA
ASY60 Benzidine Staining of Xenopus Embryo by
ASY61 Ventralization of Xenopus Embryo by RNA
ASY62 Benzidine Staining of Xenopus Embryo by
ASY63 Hematopoiesis: stem cell proliferation
ASY64 Proinflammatory/PMN Infiltrate
ASY65 HUVEC Survival in Absence of Serum
ASY66 Inhibition of Adipocyte Differentiation
ASY67 MLR - Inhibitory
Find Lots
All PIN
All DNA
Show Lots for:
LOT
Number:
2176
Include UNQ Related Lots
Lots for Search
PIN996-1
Remove All
All Positives
Verified Positives
Pending
Date Complete From
To
PIN Search
DNA Search
Reset
ASSAY RESULT LIST
Rows 1 - 4 of 4
Page 1 of 1
Select Page Page No. 1
ASY
ASY Name
PUR/E/P/DNA
LOT
LOT Name
Pos
Verified
Conc
Conc Unit
Mean
Ctrl
UNQ
Protein Name
Date Distr
Date Complete
Comment
ASY67 MLR-Inh PUR1292 LOT2176 PIN996-1 1.50 nM 63.2 UNQ316 Human MANSC1 IgG
ASY67 MLR-Inh PUR1292 LOT2176 PIN996-1 1.50 nM 77.3 UNQ316 Human MANSC1 IgG
ASY67 MLR-Inh PUR1292 LOT2176 PIN996-1 15.00 nM 64.7 UNQ316 Human MANSC1 IgG
ASY67 MLR-Inh PUR1292 LOT2176 PIN996-1 15.00 nM 99.4 UNQ316 Human MANSC1 IgG
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